Day : Thursday
Date: 4/1/2004
Time: 17:43:59

PALM INTRANET

Continuity Information for 60/150878

Parent Data
No Parent Data

"3-6"

Child Data
09519976 Claims Priority from Provisional Application 60150878
09628840 is a continuation in part of 09519976
09629587 is a continuation in part of 09519976
09629634 is a continuation in part of 09519976
09630022 is a continuation in part of 09519976
09645145 is a continuation in part of 09519976
09645146 is a continuation in part of 09519976
09645148 is a continuation in part of 09519976
09648490 Claims Priority from Provisional Application 60150878
~~09648497 Claims Priority from Provisional Application 60150878~~ #6
09649447 Claims Priority from Provisional Application 60150878 → OPB
10057659 is a continuation of 09645145
10189659 is a continuation of 10057659
10431019 is a continuation of 10189659
10434259 is a continuation of 10189659
10439438 is a continuation of 10189659
10439865 is a continuation of 10189659
PCT/US00/23363 is a continuation of 09519976
PCT/US00/23368 Claims Priority from Provisional Application 60150878

Appln Info | Contents | Petition Info | Atty/Agent Info | Continuity Data | Foreign Data

Search Another: Application# [ ] Search or Patent# [ ] Search
PCT / [ ] / [ ] Search or PG PUBS # [ ] Search
Attorney Docket # [ ] Search
Bar Code # [ ] Search

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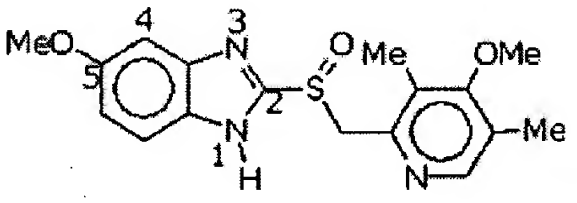
aaiPharma®
DEVELOPING CHEMISTRY INTO MEDICINE

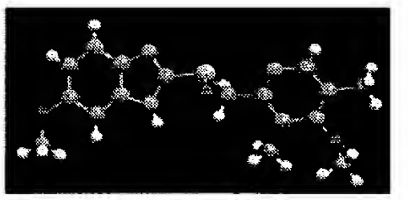
The Gastroenterology

aaiPharma Discovery Research on Omeprazole

Omeprazole

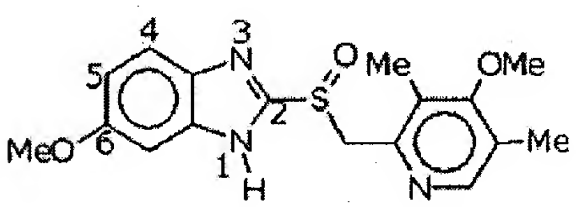
Omeprazole is a proton pump inhibitor that is used to treat acid reflux disease and gastric ulcers. Prior to work performed in *aaiPharma's* laboratories, **omeprazole** was thought to be the 5-methoxy isomer:





Omeprazole
(single crystal x-ray structure computed by *aaiPharma*)

Thorough single crystal X-ray crystallographic analysis *aaiPharma's* scientists revealed the predominant isomer in the solid state was not the expected 5-methoxy isomer, but rather the **6-methoxy** isomer:



However, when the crystal structure of the **6-methoxy** isomer was refined, a small residual electron density about the ipso carbon of the 5-benzimidazole position was noted. Taking into cognizance the possiblity of disorder within the crystal lattice, the *aaiPharma* Research Sciences team discovered that **omeprazole** is really a co-crystallized mixture of both 5- and **6-methoxy** isomers. This discovery, along with the discovery of how to prepare, control, and quantify the isomeric ratio has resulted in an impressive suite of patents.

Research scientists at *aaiPharma* discovered some surprising consequences of the 5-/**6-methoxy** isomeric composition of **omeprazole**. Most importantly, the greater the amount of the 5-methoxy isomer, the faster the **omeprazole** sample degrades. Consequently, *aaiPharma* has developed a pure **6-methoxy omeprazole** in order to provide the patient with the most stable form of the drug.

Ecabet

R & D

- Therapeutic Showcase
  - Pain and Inflammation
  - Gastroenterology
  - Critical Care
- Pipeline
- Drug Delivery
- Intellectual Property
- Publications

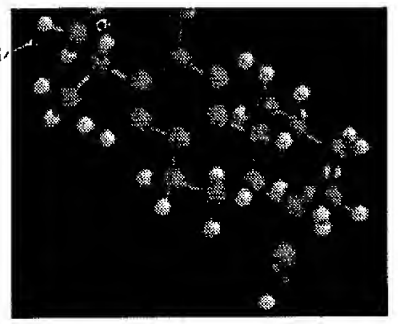
News Releases

March 15, 2004
aaiPharma Files for Form 10-K Filing Extension

March 1, 2004
aaiPharma Board of Directors Announces Independent Inquiry

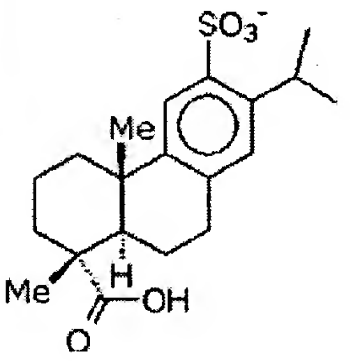
March 1, 2004
aaiPharma to Sell M.V.I.® Proc Business to Mayne Pharma USA

Contact Us



Ecabet
(single crystal x-ray structure computed by *aaiPharma*)

Ecabet is indicated for the treatment of mucosal lesions of the gastrointestinal tract and is currently marketed in Japan for treating gastric ulcers.



In the U.S. market it has been estimated that up to one million Americans suffer with inflammatory bowel disease (IBD) with approximately 30,000 new cases reported each year. Inflammatory bowel disease is divided approximately in half with one group suffering from ulcerative colitis (UC) and the other half with Crohn's disease. These diseases often first appear in the young to late teens with individuals often characterized by alternating periods of active disease alternating with periods of remission.

Ecabet appears to have multiple possible mechanisms of action mediating its therapeutic effect. Studies have demonstrated preferential binding of ecabet to damaged gastrointestinal epithelium facilitating epithelial cell regrowth and repair at the site of ulceration. The underlying activity mediating repair by ecabet is likely due to anti-inflammatory activities at the damaged site, which is supported by studies indicating that ecabet inhibits 5-lipoxygenase and ultimately the production of the leukotriene LTB4. Recent unpublished data generated by *aaiPharma* expands the potential anti-inflammatory activity demonstrated by ecabet since it can modulate the activity of I B/NF B in TNF activated T-lymphocytes.

L1 ANSWER 21 OF 21 REGISTRY COPYRIGHT 2004 ACS on STN
RN 73590-58-6 REGISTRY
CN 1H-Benzimidazole, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(±)-Omeprazole**
CN 2-[[(3,5-Dimethyl-4-methoxy-2-pyridyl)methyl]sulfinyl]-5-methoxy-1H-benzimidazole
CN 5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfinyl]-1H-benzimidazole
CN Acidex
CN Antra
CN Antra MUPS
CN Audazol
CN Aulcer
CN Belmazol
CN Ceprandal
CN Desec
CN Dizprazol
CN Dudencer
CN Elgam
CN Emeproton
CN Epirazole
CN Gastrimut
CN Gastroloc
CN Gastrozole
CN Gibancer
CN H 168/68
CN Indurgan
CN Inhibitron
CN Inhipump
CN Logastric
CN Lomac
CN Losec
CN Mepral
CN Miol
CN Miracid
CN Mopral
CN Ocid
CN Omapren
CN Omebeta 20
CN Omed
CN Omedar
CN OMEP
CN Omepradex
CN Omepral
CN Omeprazen
CN **Omeprazole**
CN Omeprazon
CN Omepril
CN Omezol
CN Omezzol
CN Omid
CN Omisec
CN Omizac
CN OMP
CN Ompanyt
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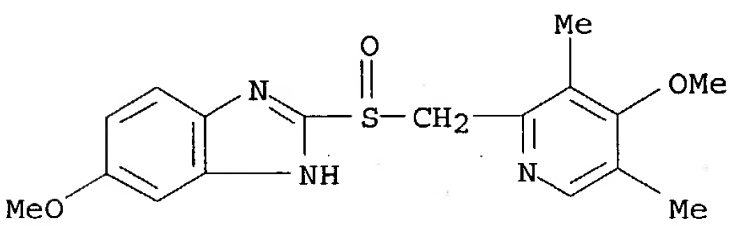
FS 3D CONCORD
DR 172964-80-6, 131959-78-9
MF C17 H19 N3 O3 S
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PIRA, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: WHO



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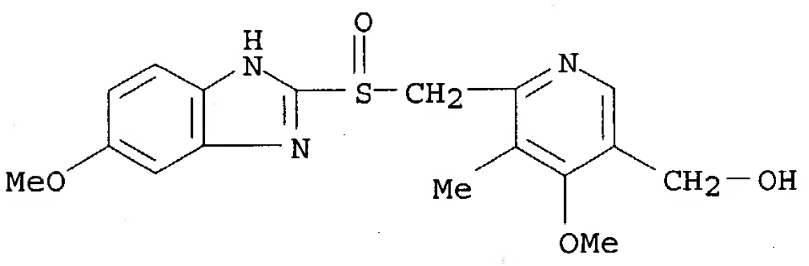
2603 REFERENCES IN FILE CA (1907 TO DATE)
47 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2613 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=>

L1 ANSWER 18 OF 21 REGISTRY COPYRIGHT 2004 ACS on STN
RN 92340-57-3 REGISTRY
CN 3-Pyridinemethanol, 4-methoxy-6-[[(5-methoxy-1H-benzimidazol-2-yl)sulfinyl]methyl]-5-methyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **5-Hydroxyomeprazole**
CN **Hydroxyomeprazole**
FS 3D CONCORD
MF C17 H19 N3 O4 S
LC STN Files: ADISNEWS, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CHEMCATS, CIN, IPA, MEDLINE, TOXCENTER, USPAT2, USPATFULL

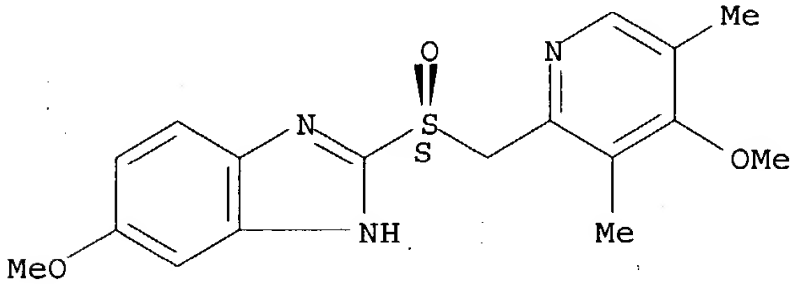


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

70 REFERENCES IN FILE CA (1907 TO DATE)
70 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 11 OF 21 REGISTRY COPYRIGHT 2004 ACS on STN
RN 119141-88-7 REGISTRY
CN 1H-Benzimidazole, 5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Benzimidazole, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-, (S)-
OTHER NAMES:
CN **(-)-Omeprazole**
CN (S)-5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfinyl]-1H-benzimidazole
CN **(S)-Omeprazole**
CN Esomeprazole
CN Nexiam
FS STEREOSEARCH
DR 193469-77-1, 326602-80-6
MF C17 H19 N3 O3 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CIN, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PROMT, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).

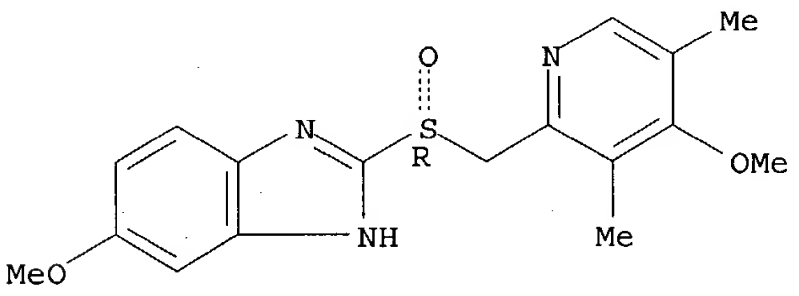


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

184 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
186 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 10 OF 21 REGISTRY COPYRIGHT 2004 ACS on STN
RN 119141-89-8 REGISTRY
CN 1H-Benzimidazole, 5-methoxy-2-[(R)-[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Benzimidazole-1-acetic acid, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-, (+)-
OTHER NAMES:
CN **(+)-Omeprazole**
CN **(R)-Omeprazole**
CN 1H-Benzimidazole, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-, (R)-
FS STEREOSEARCH
MF C17 H19 N3 O3 S
CI COM
SR CA
LC STN Files: ADISNEWS, BEILSTEIN*, CA, CAPLUS, IMSPATENTS, IMSRESEARCH, PROMT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

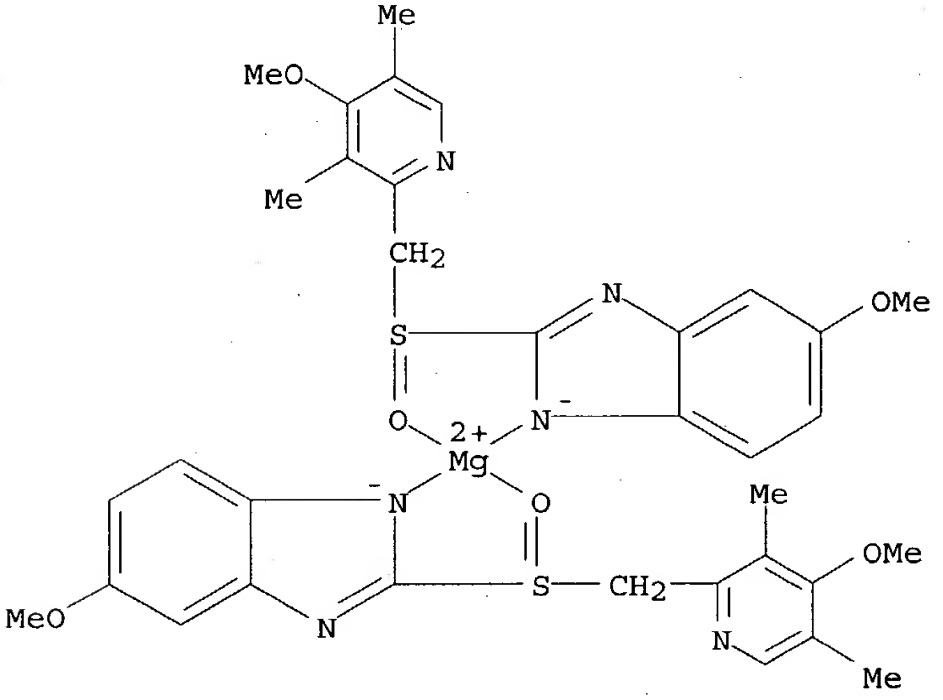
Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

58 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
59 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 7 OF 21 REGISTRY COPYRIGHT 2004 ACS on STN
RN 161973-10-0 REGISTRY
CN Magnesium, bis[5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl-κO]-1H-benzimidazolato-κN1]-, (T-4)-(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Magnesium, bis[5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazolato]-, [T-4-(S),(S)]-
OTHER NAMES:
CN **(-)-Omeprazole magnesium**
CN **(S)-Omeprazole magnesium**
CN Esomeprazole magnesium
CN H 199/18
CN Nexium
CN Perprazole
DR 502497-87-2, 202742-32-3, 302841-07-2, 320416-93-1, 371759-50-1, 372519-57-8, 376628-34-1
MF C34 H36 Mg N6 O6 S2
CI CCS, COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, DIOGENES, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PHAR, PIRA, PROMT, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)



49 REFERENCES IN FILE CA (1907 TO DATE)
50 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:814855 CAPLUS
DOCUMENT NUMBER: 137:316151
TITLE: Process for purifying **6-methoxy omeprazole**
INVENTOR(S): Whittall, Linda B.; Stowell, Grayson Walker; Whittle, Robert R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002156103	A1	20021024	US 2001-839449	20010420
US 6608091	B2	20030819		
WO 2002085312	A2	20021031	WO 2002-US15254	20020417
WO 2002085312	A3	20030403		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1379518	A2	20040114	EP 2002-736828	20020417

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

NO 2003004679	A	20031020	NO 2003-4679	20031020

PRIORITY APPLN. INFO.:
US 2001-839395 A 20010420
US 2001-839449 A 20010420
WO 2002-US15254 W 20020417

AB A processes for purifying **6-methoxy omeprazole** from 5(**6**)-**methoxy-omeprazole** by (a) rinsing 5(**6**)-**methoxy-omeprazole** with a solvent selected from a short carbon chain alc. and THF and (b) drying the product obtained is described. **6-Methoxy omeprazole** is used for pharmaceutical formulations for gastric acid inhibition. For example, the percentage of **6-methoxy omeprazole** was increased from about 67% to about 91% by rinsing 5(**6**)-**methoxy-omeprazole** twice with methanol and drying under vacuum.

L3 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:832579 CAPLUS
DOCUMENT NUMBER: 137:329531
TITLE: Process for purifying **6-methoxy omeprazole**
INVENTOR(S): Whittal, Linda; Stowell, Grayson Walker; Whittle, Robert R.
PATENT ASSIGNEE(S): Aaipharma, Inc., USA
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085312	A2	20021031	WO 2002-US15254	20020417
WO 2002085312	A3	20030403		
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US 6608091	B2	20030819		
US 2003088106	A1	20030508	US 2001-839395	20010420
US 6673936	B2	20040106		
EP 1379518	A2	20040114	EP 2002-736828	20020417
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NO 2003004679	A	20031020	NO 2003-4679	20031020

PRIORITY APPLN. INFO.:
US 2001-839395 A 20010420
US 2001-839449 A 20010420
WO 2002-US15254 W 20020417

AB The present invention provides a process for increasing the solid state percentage of **6-methoxy omeprazole** from an amount of 5(**6**)-**methoxy omeprazole** by (a) rinsing 5(**6**)-**methoxy omeprazole** with a short chain alc. solvent and THF, and (b) drying the product from step (a). Pharmaceutical formulations containing 5(**6**)-**methoxy omeprazole** are useful for gastric acid inhibition. For example, 20 mL of methanol was added to 1.8 g of 5(**6**)-**methoxy omeprazole** having about 33% of 5-methoxy isomer until the sample was substantially covered and wetted. The solvent was removed under vacuum at ambient temperature and the process was repeated one more time. After drying the product yield was 49%, and the percentage of **6-methoxy omeprazole** was increased from 67% to 91%.

L3 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:814855 CAPLUS
DOCUMENT NUMBER: 137:316151
TITLE: Process for purifying **6-methoxy omeprazole**
INVENTOR(S): Whittall, Linda B.; Stowell, Grayson Walker; Whittle, Robert R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6608091	B2	20030819		
WO 2002085312	A2	20021031	WO 2002-US15254	20020417
WO 2002085312	A3	20030403		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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EP 1379518	A2	20040114	EP 2002-736828	20020417

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

NO 2003004679	A	20031020	NO 2003-4679	20031020

PRIORITY APPLN. INFO.:

US 2001-839395	A	20010420
US 2001-839449	A	20010420
WO 2002-US15254	W	20020417

AB A processes for purifying **6-methoxy omeprazole** from 5(**6**)-**methoxy**-**omeprazole** by (a) rinsing 5(**6**)-**methoxy**-**omeprazole** with a solvent selected from a short carbon chain alc. and THF and (b) drying the product obtained is described. **6-Methoxy omeprazole** is used for pharmaceutical formulations for gastric acid inhibition. For example, the percentage of **6-methoxy omeprazole** was increased from about 67% to about 91% by rinsing 5(**6**)-**methoxy**-**omeprazole** twice with methanol and drying under vacuum.

L3 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:832579 CAPLUS
DOCUMENT NUMBER: 137:329531
TITLE: Process for purifying **6-methoxy omeprazole**
INVENTOR(S): Whittal, Linda; Stowell, Grayson Walker; Whittle, Robert R.
PATENT ASSIGNEE(S): Aaipharma, Inc., USA
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085312	A2	20021031	WO 2002-US15254	20020417
WO 2002085312	A3	20030403		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002156103	A1	20021024	US 2001-839449	20010420
US 6608091	B2	20030819		
US 2003088106	A1	20030508	US 2001-839395	20010420
US 6673936	B2	20040106		
EP 1379518	A2	20040114	EP 2002-736828	20020417
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2003004679	A	20031020	NO 2003-4679	20031020

PRIORITY APPLN. INFO.:

US 2001-839395	A	20010420
US 2001-839449	A	20010420
WO 2002-US15254	W	20020417

AB The present invention provides a process for increasing the solid state percentage of **6-methoxy omeprazole** from an amount of 5(**6**)-**methoxy omeprazole** by (a) rinsing 5(**6**)-**methoxy omeprazole** with a short chain alc. solvent and THF, and (b) drying the product from step (a). Pharmaceutical formulations containing 5(**6**)-**methoxy omeprazole** are useful for gastric acid inhibition. For example, 20 mL of methanol was added to 1.8 g of 5(**6**)-**methoxy omeprazole** having about 33% of 5-methoxy isomer until the sample was substantially covered and wetted. The solvent was removed under vacuum at ambient temperature and the process was repeated one more time. After drying the product yield was 49%, and the percentage of **6-methoxy omeprazole** was increased from 67% to 91%.

L3 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:152490 CAPLUS
DOCUMENT NUMBER: 134:198192
TITLE: FT-Raman spectroscopic measurement of **omeprazole** isomer ratio in a composition
INVENTOR(S): Whittle, Robert R.; Sancilio, Frederick D.; Stowell, Grayson Walker
PATENT ASSIGNEE(S): Applied Analytical Industries, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001013919	A1	20010301	WO 2000-US23368	20000823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,				

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000069377	A5	20010319	AU 2000-69377	20000823	
EP 1206263	A1	20020522	EP 2000-957808	20000823	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003507721	T2	20030225	JP 2001-518056	20000823	
ZA 2002001519	A	20030522	ZA 2002-1519	20020222	
ZA 2002001521	A	20030522	ZA 2002-1521	20020222	

PRIORITY APPLN. INFO.:
US 1999-150878P P 19990826
WO 2000-US23368 W 20000823

AB Fourier-transform Raman spectroscopy (FT-Raman) dets. the isomer ratio of chemical compns., especially the ratio of 5(6)-**methoxy** isomers of **omeprazole**. An **omeprazole** active pharmaceutical ingredient (API) composition fixed with a ratio of 5(6)-**methoxy** isomers is also disclosed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:875245 CAPLUS
DOCUMENT NUMBER: 136:11182
TITLE: Dry blend of methoxybenzimidazole derivs. for oral dosage forms
INVENTOR(S): Whittle, Robert R.; Sancilio, Frederick D.; Stowell, Grayson Walker; Jenkins, Douglas John; Whittall, Linda B.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 39 pp., Cont.-in-part of U.S. 6,262,085.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6326384	B1	20011204	US 2000-645148	20000824
US 6262085	B1	20010717	US 2000-519976	20000307

PRIORITY APPLN. INFO.: US 1999-150878P P 19990826
US 2000-519976 A2 20000307
OTHER SOURCE(S): MARPAT 136:11182

AB The present invention provides dry blend pharmaceutical formulations in unit dosage forms comprising per dosage unit one or more active pharmaceutical ingredients or pharmaceutically acceptable salts, solvates, hydrates, or combinations thereof wherein the **ratio** of said one or more active pharmaceutical ingredients in said formulations is essentially the same as the **ratio** of said active pharmaceutical ingredients in the corresponding, non-formulated drug substance and, wherein said formulations in unit dosage form are adapted for oral administration in a form of a capsule or a tablet. The active pharmaceutical ingredient is 4-methoxy-3,5-dimethyl-2-pyridinyl or one or more pharmaceutically acceptable salts, solvates, hydrates, or combinations thereof, in pure form or essentially free of **5-methoxy**-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole. For example, a tablet formulation was manufactured by complexing 5(**6**)-**methoxy**-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole (I) with hydroxypropyl-β-cyclodextrin (HPβCD) in solution and spraying the solution onto lactose. The spray on lactose material was then blended with excipients and compressed into core tablets. The formulation contained I 20.0 mg, HPβCD 80.0 mg, lactose 68.7 mg, magnesium stearate 0.4 mg, and colloidal silica 0.4 mg per tablet. Tablets were coated to a 4.5% total solids weight gain with an Opadry White coating solution as a subcoat. After drying, a 10% total solids weight gain from an Eudragit L 30 or D-55 coating solution was applied as an enteric coat.

REFERENCE COUNT: 147 THERE ARE 147 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:828927 CAPLUS
DOCUMENT NUMBER: 135:362587
TITLE: Cyclodextrin-containing pharmaceutical formulations for benzimidazole derivatives
INVENTOR(S): Whittle, Robert R.; Sancilio, Frederick D.; Stowell, Grayson Walker; Jenkins, Douglas John; Whittall, Linda B.; Meyer, Glenn Alan
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 36 pp., Cont.-in-part of U.S. 6,202,085.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6316020	B1	20011113	US 2000-629587	20000731
US 6262085	B1	20010717	US 2000-519976	20000307

PRIORITY APPLN. INFO.: US 1999-150878P P 19990826
US 2000-519976 A2 20000307
OTHER SOURCE(S): MARPAT 135:362587
AB Pharmaceutical compns. comprise a benzimidazole derivative as an active ingredient or a pharmaceutically acceptable salt, solvate, hydrate, or their combinations with at least one cyclodextrin and at least one pharmaceutically acceptable carrier, diluent, or excipient. For example, to a 50 mL beaker about 1 g of 5(**6**)-**methoxy**-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole was added to 30 mL of methylene chloride. Addnl. 5(**6**)-**methoxy**-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole was added to the resulting solution until a suspension of the material was formed. The solution was stirred for approx. 10 min, and then filtered through a 0.45 μm PTFE or Nylon filter. The resulting saturated solution was placed in a beaker, covered, and stored under refrigerated conditions (approx. 5°) until crystals formed (between 1-2 days). The identity of the title compound was confirmed by single crystal x-ray diffraction and/or Raman spectroscopy. The resulting material was determined to contain about 84-88% (weight/weight) of the **6-methoxy**-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole and about 12-16% (weight/weight) (I) of the **5-methoxy**-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole (II). I and II were formulated in various dosage forms, such as tablets, capsules, enteric-coated tablets, and solns. for inhibiting gastric acid secretion. The formulations contained a cyclodextrin, e.g. hydroxypropyl β-cyclodextrin, in a drug to cyclodextrin **ratio** of 1:4-1:20 to increase drug solubility
REFERENCE COUNT: 147 THERE ARE 147 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:152490 CAPLUS
DOCUMENT NUMBER: 134:198192
TITLE: FT-Raman spectroscopic measurement of **omeprazole isomer ratio** in a composition
INVENTOR(S): Whittle, Robert R.; Sancilio, Frederick D.; Stowell, Grayson Walker
PATENT ASSIGNEE(S): Applied Analytical Industries, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001013919	A1	20010301	WO 2000-US23368	20000823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000069377	A5	20010319	AU 2000-69377	20000823
EP 1206263	A1	20020522	EP 2000-957808	20000823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003507721	T2	20030225	JP 2001-518056	20000823
ZA 2002001519	A	20030522	ZA 2002-1519	20020222
ZA 2002001521	A	20030522	ZA 2002-1521	20020222

PRIORITY APPLN. INFO.: US 1999-150878P P 19990826
WO 2000-US23368 W 20000823

AB Fourier-transform Raman spectroscopy (FT-Raman) dets. the **isomer ratio** of chemical compns., especially the **ratio** of 5(**6**)-**methoxy isomers** of **omeprazole**. An **omeprazole** active pharmaceutical ingredient (API) composition fixed with a **ratio** of 5(**6**)-**methoxy isomers** is also disclosed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:592034 CAPLUS
DOCUMENT NUMBER: 136:288376
TITLE: Pharmacokinetic studies with esomeprazole, the (S)-**isomer** of **omeprazole**
AUTHOR(S): Andersson, Tommy; Hassan-Alin, Mohammed; Hasselgren, Goran; Rohss, Kerstin; Weidolf, Lars
CORPORATE SOURCE: AstraZeneca LP, Wayne, PA, USA
SOURCE: Clinical Pharmacokinetics (2001), 40(6), 411-426
CODEN: CPKNDH; ISSN: 0312-5963
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. This article reviews the pharmacokinetics of esomeprazole, the (S)-**isomer** of the proton pump inhibitor (PPI) **omeprazole**. Esomeprazole is the first single **isomer** PPI developed for the treatment of patients with acid-related diseases. In

vitro expts. in human liver microsomes demonstrated that the formation of the hydroxy and 5-O-desmethyl metabolites of esomeprazole is via cytochrome P 450 (CYP) 2C19, whereas that of the sulfone metabolite is via CYP3A4. The formation rate of the hydroxy metabolite from esomeprazole is lower than for (R)-**omeprazole**, but that of the 2 other metabolites is higher, demonstrating stereoselective metabolism The sum of the intrinsic clearances of all 3 metabolites for esomeprazole was one-third of that for (R)-**omeprazole**, suggesting lower clearance of esomeprazole in vivo. In vivo investigations demonstrated that esomeprazole is chirally stable after administration. Esomeprazole is 97% bound to plasma proteins. In normal (extensive) metabolizers with regard to CYP2C19, esomeprazole is metabolized more slowly than **omeprazole**, resulting in a higher area under the concentration-time curve (AUC) after administration of the same dose. This is more pronounced after repeated administration rather than after a single dose. In poor metabolizers, the AUC is lower for esomeprazole than for **omeprazole**, contributing to less overall interindividual variability for esomeprazole than for **omeprazole**. In general, esomeprazole and **omeprazole** are subject to the same metabolic transformations. Almost complete recoveries were reported and the **ratio** between urinary and fecal excretion is about 4:1 for both compds. The dose-dependent increase in AUC of esomeprazole with repeated administration results from a combination of decreased first-pass elimination and decreased systemic clearance. Patients with gastro-esophageal reflux disease exhibit a pharmacokinetic pattern similar to that in healthy individuals, whereas elderly individuals exhibited a slightly lower metabolism rate. Patients with a severe deficit in their liver function had a lower rate of metabolism, as would be expected, whereas those with mild to moderate liver disease did not exhibit any alteration in the pharmacokinetics. The pharmacokinetics of esomeprazole in individuals with impaired renal function is unlikely to differ from that in healthy individuals. A slight sex difference in the pharmacokinetics of esomeprazole was demonstrated in that the AUC and peak plasma drug concentration were slightly, but not statistically significantly, higher in females than in males.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s omeprazole and (5-methoxy or 6-methoxy or tautomer or isomer)
L4          314 OMEPRAZOLE AND (5-METHOXY OR 6-METHOXY OR TAUTOMER OR ISOMER)

=> s l4 and ratio
L5           19 L4 AND RATIO

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6           10 DUP REM L5 (9 DUPLICATES REMOVED)

=> focus
PROCESSING COMPLETED FOR L6
L7           10 FOCUS L6 1-

=> d ibib abs 1-10
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